AP-PRE-REQ-

ONCOSIS.005A PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Koller et al.
Appl. No.	:	10/698,343
Filed	:	October 31, 2003
For	:	METHOD AND APPARATUS FOR CELL PERMEABILIZATION
Examiner	:	Fernandez, Susan Emily
Group Art Unit	:	1651

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July 27, 2006
(Date)

Marc T. Morley, Reg. No. 52,051

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicants request review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reasons stated in the accompanying Remarks, which begin on page 2 of this paper.

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REMARKS

Claims 1-18, 21-34 and 45-56 are pending. Claims 1, 48 and 56 are the independent claims. All pending claims were finally rejected in the Final Office Action mailed on January 27, 2006 as being either indefinite under 35 U.S.C. § 112, ¶2, as anticipated under 35 U.S.C. § 102 or as being obvious under 35 U.S.C. § 103. As explained below, Applicants request pre-appeal brief review of the pending rejections.

Concise Statement of Reasons for Review

Review of Anticipation and Obviousness Rejections in View of Kasuya et al.

Applicants respectfully request review of the rejection of Claims 1, 6-9, 14, 17-18, 23, 25-29, 32, 45-48, 51, 55 and 56 under 35 U.S.C. § 102(b) as being anticipated by Kasuya et al. (U.S. Patent No. 5,013,660; issued May 7, 1991). Applicants also request review of the rejection of Claims 1-18, 21-34 and 45-56 under 35 U.S.C. § 103(a) over Kasuya et al. in view of various secondary references.

In formulating the rejections, the Examiner argues that Kasuya et al. discloses a method where there is no "prior knowledge of the location of" the cells (Claim 1) or no "prior knowledge of the specific three-dimensional location of" the cells (Claims 48 and 56). With respect to Claim 1, the Examiner argues that Example 1 of Kasuya et al. describes an embodiment in which there is no knowledge of the location of the cells.

With respect to Claims 48 and 56, the Examiner argues that in the discussion of Figure 4 on column 5 of Kasuya et al., the only information obtained is the planar distribution of the cells without any specifics in terms of coordinates. Therefore, the Examiner asserts that column 5 describes a method in which the two-dimensional coordinates are known, but not the three-dimensional coordinates. Therefore, the Examiner argues that the method of Kasuya et al. does not have knowledge of the three-dimensional location of the cell(s).

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). Similarly, in order to be obvious, the combination of prior art references must teach or suggest every limitation of the claims. The Federal Circuit has declared that "it is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art." *Bausch & Lomb v. Barnes-Hind/Hydrocurve,*

796 F.2d 443, 448 (Fed. Cir. 1986) (quoting *In re Wesslau*, 353 F.2d 238, 241 (CCPA 1965)); see also *In re Mercer*, 515 F.2d 1161 (CCPA 1975). In *Bausch & Lomb*, the Court of Appeals rejected the district court's obviousness determination, stating that the lower court engaged in improper hindsight analysis and incorrectly took statements out of context to support its conclusions. *Id.* The Federal Circuit found that the district court engaged in improper hindsight analysis by viewing an isolated line in the prior art reference in light of the teaching of the patent at issue. *Id.*

Here, all of the claim limitations are not taught or suggested by Kasuya et al. either alone or in combination with the other references. The Examiner rejected the claims under §§ 102 and 103 by using impermissible hindsight from Applicants' disclosure and by choosing portions of Kasuya et al. and interpreting those portions out of context. In sum, no portion of the specification, the claims or the drawings of Kasuya et al. can be fairly read as teaching or suggesting methods of irradiating cells without knowledge of the location of the cells, unless the teachings are taken out of context or interpreted with impermissible hindsight.

Every specifically described embodiment of Kasuya et al. discloses a method where the location of a cell or cells is known prior to firing the treatment laser. There is no method described in Kasuya et al. where a cell is irradiated without knowledge of the cell's location. Parts of Kasuya et al. are silent regarding knowledge of cell location, not because the location of cells was not known, but because those parts of the reference are emphasizing other aspects of the invention.

For instance, Example 1 showed that laser-based implantation worked, which was impressive in a field where previous state-of-the-art implantation (as described in the background of Kasuya et al.) used an actual needle or a combination of chemicals to cause the cells to phagocytose the materials. Example 1 does not detail a method of irradiating a cell without knowing the location of a cell. In fact, Example 1 is silent regarding the exact details of how the cells were irradiated. The other examples in the patent provide the specific details regarding how the implantation was performed, and none or those examples describe a method where a cell is irradiated without knowledge the location of the cell. Only with the benefit of the instant application would a person view Example 1, or any other part of Kasuya et al. as teaching or suggesting irradiating without knowledge of cell location.

Figures 4-9 of Kasuya et al. depict the apparatuses used to perform the implantation methods. The operation of every one of the apparatuses in Kasuya et al. utilizes a TV monitor, a detector, and/or "spot positioning means." Not a single method is described or suggested that does not utilize

a TV, a detector, or a spot positioning means. For further detail, please see Applicants *Amendment and Response* filed on November 14, 2005 at pages 13-15.

Specific to Claim 1, the Examiner argues that Example 1 in Kasuya et al. is an embodiment where there is no knowledge of the location of the cells, only that the cells are floating in the medium. Example 1, however, does not describe irradiating cells in the medium without knowledge of their location. As mentioned above, Example 1 does not provide sufficient detail to know the method of cell irradiation. This is not surprising because presumably the purpose of Example 1 was to demonstrate for the first time the feasibility of implanting living cells with a foreign substance using a laser beam. Example 1 showed that the only cells to survive were those that were irradiated. Further, all of the cells on the left side were irradiated, while those on the right side were not. *See* Kasuya et al. Example 1, photograph. The system of Kasuya et al. did not irradiate all of the cells on one half without knowledge of the location of the cells. A more likely scenario is that the cells on one side were irradiated using the specific methods (*e.g.*, Figures 4-9 and column 5) described by Kasuya et al. where irradiation only occurred after the location of a cell was known. Reading Example 1 as teaching irradiation of cells without knowledge of the cells' location can only be done using impermissible hindsight. Absent impermissible hindsight, nobody of skill in the art of would view Example 1 as anticipating Claim 1.

In view the above comments and the arguments contained within the *Response and Amendment* filed on November 14, 2005, Applicants respectfully request reconsideration and withdrawal of the § 102 and § 103 rejections of Claim 1.

With regard to Claims 48 and 56, the Examiner argues that Kasuya et al. at column 5, lines 32-37 describes a method where there is no knowledge of the three-dimensional location of a cell. The referenced passage is part of the description of the apparatus of Figure 4. The apparatus illustrated in Figure 4 functions using a method wherein the three-dimensional location of a cell is known. The discussion of Figure 4 describes a "sweeping" method that includes the use of two laser beams, a reference laser beam 10 and a punching laser beam 2. *See* Kasuya et al. at column 5, lines 20-26. A shutter 5 is closed and prevents the punching beam from striking the cells until a cell is located. *See* column 5, lines 40-44. The reference laser sweeps the cell sample acting as a pilot to indicate where the punching laser will strike. *See id.* The stage holding the cell sample is moved along the X-Y plane while the reference laser sweeps the sample acting as a pilot. When a cell or group of cells appears in the field of the TV monitor, the shutter is opened and the punching laser beam strikes the cells at the location indicated by the reference laser. Thus, the reference laser is

focused on a specific known Z coordinate. *See* column 5, lines 40-48. The Z coordinate remained fixed while the X-Y coordinates were varied as the stage/cell sample was moved. Therefore, in the method described in column 5 of Kasuya et al., the specific three-dimensional location of a cell was known before the cell was irradiated.

In view of the above discussion and the comments from the *Response and Amendment* filed on November 14, 2005 at pages 13-15, Applicants request reconsideration of the § 102 and § 103 rejections.

Review of Indefiniteness Rejections

Applicants request review of the indefiniteness rejections of the claims. Applicants incorporate their previous arguments from the *Response and Amendment* filed on November 14, 2006 at pages 9-13.

Review of the indefiniteness rejection of Claims 1, 48 and 56 is requested. The Examiner rejected Claims 1, 48 and 56 under 35 U.S.C. § 112, ¶ 2 as being indefinite due to recitation of "without prior knowledge of the location of said one or more cells" (Claim 1) and "without prior knowledge of the specific three-dimensional location of said one or more cells" (Claims 48 and 56). According to the Examiner the phrases are confusing. Applicants disagree.

One of skill in the art would find the rejected passages clear and definite. Nonetheless, Applicants again clarify that the position of the vessel or container of the cell(s) is known, however, the specific three-dimensional position of any given cell may not be known prior to directing the electromagnetic to a location within the cell containment device. As one example, paragraph [0121] states "[a]n area of the well was exposed to a predetermined grid pattern of laser shots that did not require locating the target cells prior to shooting." Therefore, the electromagnetic radiation was directed to a location of the cell containment device without knowing if a cell was at the particular location. Thus, the phrase "without prior knowledge" is clear and definite in view of the specification.

Applicants request review of Claims 45, 48 and 56, which were rejected as indefinite for recitation of "effective distance." The phrase, "effective distance" is defined in the specification in paragraph [0073]. In relevant part paragraph [0073] states "the effective distance is a predetermined distance within which the electromagnetic radiation is known to be effective for the purpose of inducing transient permeability in a cell." A given beam of radiation has characteristics that determine how close it must come to a cell to induce transient permeabilization. For example, some

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beams must directly contact a cell at a particular angle or at the exact focal point of the beam in order to be cause permeabilization. Although other beams may have a diameter or energy density so that the beam does not have to directly contact the cell, but only irradiate in the vicinity of the cell to induce permeabilization. One of skill in the art would understand the meaning of the phrase "effective distance" and can easily determine the effective distance for a given electromagnetic radiation beam. Thus, the phrase "effective distance" is clear and definite to the skilled artisan.

Furthermore, Applicants request review of the rejection of Claims 47 and 56 as being indefinite for use of the term "substantially." Please see the *Response and Amendment* filed on November 14, 2005 at pages 10 and 11. Finally, Applicants request review of the rejection of Claims 16 and 18 for use of the phrase "modified nucleic acid." The phrase is a term of art that is understood by those of skill in the art. Thus, for this reason and for the reasons set forth in the *Response and Amendment* filed on November 14, 2005 at page 12, reconsideration and withdrawal of the indefiniteness rejection of Claims 16 and 18 is requested.

Conclusion

Applicants have requested review of and have address each of the pending rejections. If after review, the panel should find any remaining impediment to allowing one or more of the claims, Applicants respectfully request that the panel decision specifically address any such remaining rejection(s) to permit Applicants to determine any necessary follow up actions.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 27, 2006

By: _____

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